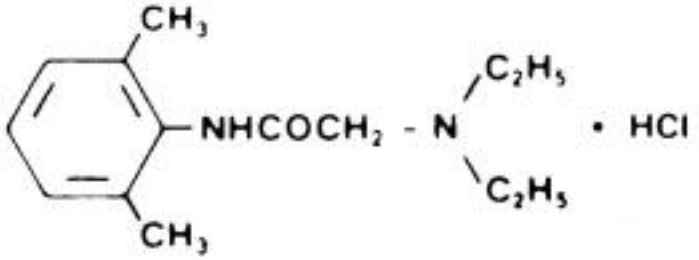
LIDOPEN - lidocaine hydrochloride injection
MERIDIAN MEDICAL TECHNOLOGIES, INC.

DESCRIPTION

Lidocaine hydrochloride: acetamide, 2-(diethylamino)-N-(2, 6-dimethylphenyl)-, monohydrochloride has the following structural formula:

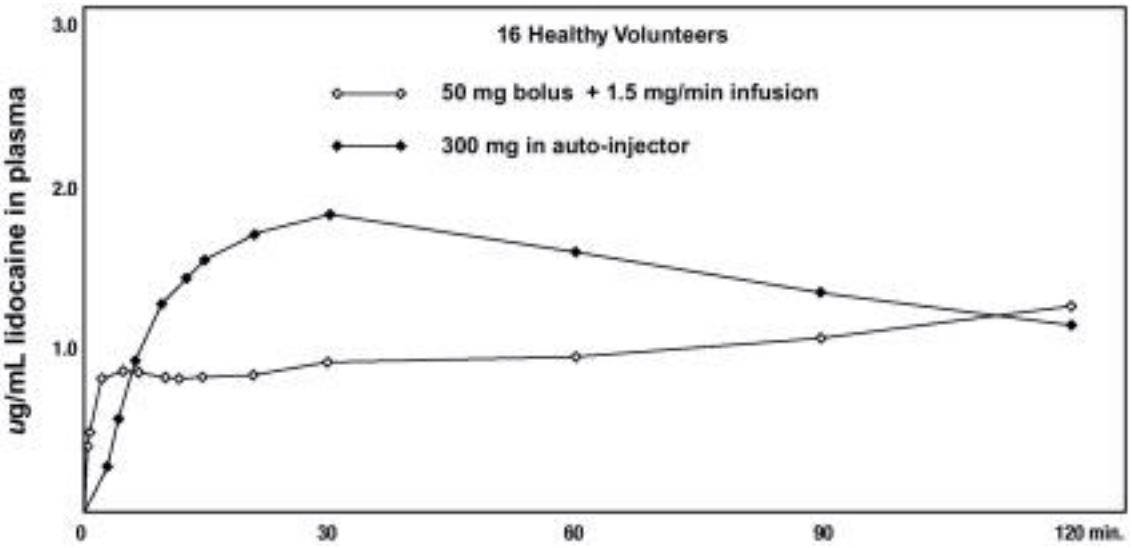


Lidocaine Hydrochloride Injection, intramuscular for Cardiac Arrhythmias, is a non-pyrogenic, sterile solution prepared from lidocaine hydrochloride, USP and Water for Injection. Lidocaine hydrochloride: $C_{14}H_{22}N_2O$ • HCI • H_2O has a molecular weight of 288.82.

Each LidoPen® contains 300 mg lidocaine hydrochloride, 3 mg disodium edetate, 3 mg methylparaben, sodium hydroxide in sufficient quantity to adjust pH to 5.2 in 3.0 mL Water for Injection.

CLINICAL PHARMACOLOGY

Lidocaine hydrochloride is reported to increase the electrical stimulation threshold of the ventricle during diastole and, thereby, exert an antiarrhythmic effect. In the dosage recommended, lidocaine hydrochloride produces no change in systolic arterial blood pressure, absolute refractory period, or myocardial contractility.



Clinical studies in which cardiac arrhythmias were monitored indicated that the onset and duration of antiarrhythmic activity of intramuscular lidocaine hydrochloride are correlated with the attained blood levels of lidocaine hydrochloride.

The relative blood levels in normal volunteers obtained by a “conventional” intravenous infusion and following the LidoPen® Auto-Injector can be determined by reference to the accompanying chart.

Approximately 90% of an administered dose of lidocaine hydrochloride is metabolized in the liver. Less than 10% of the drug is excreted unchanged via the kidneys.

INDICATIONS AND USAGE

Lidocaine hydrochloride is indicated in the management of cardiac arrhythmias, particularly those of ventricular origin, such as occur with acute myocardial infarction.

The selection of the intramuscular route of administration (single dose) is justified in the following circumstances:

1. By a physician in whose opinion the potential benefits outweigh the possible risks even when ECG equipment is not available to verify the arrhythmia.

2. By, or under the supervision of, a physician, including mobile coronary care units, when facilities for intravenous administration are not readily available, or under circumstances where maintaining continuous intravenous therapy is difficult or impossible.

3. For use in the pre-hospital phase of suspected acute myocardial infarction by a patient who has transmitted his electrocardiogram with a CardioBeeper®, whose electrocardiogram demonstrates the presence of a ventricular arrhythmia and who is instructed by qualified medical personnel to self-administer the LidoPen® Auto-Injector.

CONTRAINDICATIONS
Lidocaine hydrochloride is contraindicated in patients with known hypersensitivity to local anesthetics of the amide type, in patients with STOKES-ADAMS Syndrome, Wolff-Parkinson-White Syndrome, or severe degrees of sinoatrial, atrio-ventricular, or intraventricular block.

WARNINGS
EVERY EFFORT SHOULD BE MADE TO AVOID POSSIBLE INADVERTENT INTRAVASCULAR ADMINISTRATION THROUGH APPROPRIATE SELECTION OF INJECTION SITE SUCH AS THIGH OR DELTOID. DO NOT INJECT INTO BUTTOCK. Monitoring with an electrocardiograph is recommended when lidocaine hydrochloride is administered by the intramuscular route. In emergency situations when a ventricular rhythm disorder is suspected and electrocardiographic equipment is not available, a single dose may be administered when the physician in attendance has determined that the potential benefits outweigh the possible risks. If possible, emergency resuscitative equipment and drugs should be immediately available to manage potential adverse reactions involving the cardiovascular, respiratory, or central nervous system.
Occasional acceleration of ventricular rate may occur when lidocaine hydrochloride is administered to patients with atrial fibrillation.

PRECAUTIONS

General:
Caution should be employed in the repeated use of lidocaine hydrochloride in patients with severe liver or renal disease because accumulation may occur and lead to toxic phenomena since lidocaine hydrochloride is metabolized mainly in the liver and excreted by the kidneys. This drug should also be used with caution in patients with hypovolemia and shock and all forms of heart block.
Half-life and clearance of lidocaine are reduced, when administered to patients on propranolol. A recent study indicates that half-life was prolonged from 65 to 101 minutes and clearance was reduced from 18.0 to 10.7 mL/min/kg after single administration of lidocaine. The clearance of lidocaine was further reduced during continuous infusion. These factors should be considered when the LidoPen® Auto-Injector is prescribed and during use of lidocaine in patients on propranolol. See **CONTRAINDICATIONS** and **WARNINGS.**

Information for Patient:
A separate booklet containing patient information and instructions for self-administration is provided. The full text of the booklet is reprinted in **DETAILED INSTRUCTIONS** section.

Under no circumstances should the LidoPen® Auto-Injector be used without specific instructions to do so by qualified medical personnel.
Unless absolutely necessary, do not attempt to operate a motor vehicle after use.

Drug Interactions:
Caution should be exercised in administration to patient with known or suspected digitalis toxicity accompanied by atrioventricular block. See**CONTRAINDICATIONS.**
Many potent anesthetic drugs, neuromuscular blocking agents and possible amide local anesthetics may serve as triggering agents for the fulminant hypermetabolic process termed malignant hyperthermia.

Drug/Laboratory Test Interactions:
The intramuscular use of lidocaine hydrochloride may result in an increase in creatine phosphokinase levels. Thus, the use of the enzyme determination without isoenzyme separation, as a diagnostic test for the presence of acute myocardial infarction, may be compromised by the use of intramuscular lidocaine hydrochloride.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

Usage in Pregnancy:
Pregnancy Category B: Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus due to lidocaine.
There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Pediatric Use:
Intramuscular lidocaine hydrochloride should not be used in children under 50 kg (110 lbs).

ADVERSE REACTIONS

The following types of systemic reactions have been reported with lidocaine hydrochloride administration:

1. Central Nervous System: light-headedness; drowsiness; dizziness; apprehension; euphoria; tinnitus; blurred or double vision; vomiting; sensations of heat, cold or numbness; twitching; tremors; convulsions; unconsciousness; respiratory depression and arrest.

2. Cardiovascular System: hypotension; bradycardia; cardiovascular collapse and cardiac arrest.

3. Allergic reactions may occur but are infrequent. There have been no reports of cross-sensitivity between lidocaine hydrochloride and procainamide or between lidocaine hydrochloride and quinidine.

Soreness at the injection site following intramuscular injection has occasionally been reported.

MANAGEMENT OF ADVERSE REACTIONS

1. In the case of severe reaction, do not continue or repeat administration of the drug.

2. Institute emergency resuscitative procedures including maintenance of patent airway and cardiopulmonary resuscitation, if required.

3. For severe convulsions, parenteral administration of a rapidly acting anticonvulsant may be used by persons appropriately trained in the use of those drugs and the management of the cardiovascular and respiratory depression which may result. Resuscitative equipment should be available.

OVERDOSAGE

Reactions due to overdosage are generally systemic in nature and involve the central nervous system and the cardiovascular system. See **ADVERSE REACTIONS**.

Should convulsions or signs of respiratory depression and arrest develop, the patency of the airway and adequacy of ventilation must be assured immediately. See **MANAGEMENT OF ADVERSE REACTIONS**.

The approximate oral LD50 of lidocaine hydrochloride in mice is 520 mg/kg. Plasma levels in excess of 8 mcg/mL in humans have been associated with serious adverse effects.

Dialysis is of negligible value in the treatment of acute overdosage from lidocaine hydrochloride.

DOSAGE AND ADMINISTRATION

A physician who prescribes this device for the patient, must take appropriate steps to insure that his patient understands the indications and use of this device including review with the patient, in detail, the patient package insert and operation of the Auto-Injector.

Inject the contents of 1 LidoPen® Auto-Injector (300 mg lidocaine hydrochloride, 3 mL, 10% solution) intramuscularly into the anterolateral aspect of the thigh or deltoid region of the arm. See **DETAILED INSTRUCTIONS** below.

As soon as possible, and when indicated, patients should be changed to an intravenous infusion of lidocaine hydrochloride or to an oral antiarrhythmic preparation for maintenance therapy. However, if necessary, an additional intramuscular injection may be made after an interval of 60-90 minutes. IT SHOULD BE MADE CLEAR TO THE PATIENT THAT THIS SECOND INJECTION SHOULD NOT BE MADE WITHOUT FURTHER INSTRUCTIONS BY QUALIFIED MEDICAL PERSONNEL.

DETAILED INSTRUCTIONS

NOTE: A separate booklet containing information regarding self-administration of the LidoPen® Auto-Injector by patients equipped with a CardioBeeper® will be made available to the patient.

Introduction:

As part of the early management of a heart attack, your physician has prescribed for you a drug — lidocaine hydrochloride contained in an automatic injector — The LidoPen® Auto-Injector.

This drug has been shown to be valuable in the management of certain abnormal heart rhythms which sometimes accompany heart attacks. As with all other drugs, it is not without risk. UNDER NO CIRCUMSTANCES SHOULD IT BE USED WITHOUT SPECIFIC INSTRUCTIONS TO DO SO BY QUALIFIED MEDICAL PERSONNEL.

Therefore, your physician has taken steps to provide you with a CardioBeeper® with which to transmit your heart rate and rhythm by conventional telephone.

Be certain to review the information contained in this booklet and practice with the use of the CardioBeeper®.

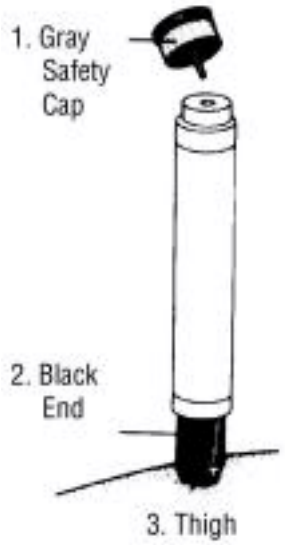
The LidoPen® Auto-Injector:
The LidoPen® Auto-Injector is a disposable, prefilled automatic injection device containing 300 mg lidocaine hydrochloride.

- Keep the LidoPen® Auto-Injector with you at all times.
- It should not be kept in excessive heat or cold.
- You should note the expiration date on the LidoPen® Auto-Injector and make sure yours is replaced prior to that date.

When to use the LidoPen® Auto-Injector:
If you experience the signs and symptoms described to you by your physician as suggesting a possible heart attack, immediately telephone your physician, or center designated by your physician, and transmit your electrocardiogram by CardioBeeper®. You will then be instructed whether or not you are to use the LidoPen® Auto-Injector.

Directions for Use:
When as described above, you have been instructed to use the LidoPen® Auto-Injector, proceed as follows:

1. Remove gray safety cap.
2. Place black end on thickest part of thigh and press hard until injector functions.
3. Hold firmly in place for ten seconds, then remove. Massage the area of injection for 10 seconds.



UNLESS ABSOLUTELY NECESSARY, DO NOT ATTEMPT TO OPERATE A MOTOR VEHICLE AFTER USE OF THE LidoPen® Auto-Injector.

Proceed as instructed by physician.

HOW SUPPLIED

Each LidoPen® Auto-Injector contains 300 mg lidocaine hydrochloride, 3 mg disodium edetate, 3 mg methylparaben, sodium hydroxide in sufficient quantity to adjust pH to 5.2 in 3.0 mL Water for Injection NDC 11704-221-02. Store at room temperature (15°-30°C/59°-86°F).
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